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COMPARISON OF ACID NEUTRALIZING AND NON-ACID NEUTRALIZING STRESS ULCER PROPHYLAXIS IN THERMALLY INJURED PATIENTS

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We have compared the effectiveness of non-acid neutralizing stress ulcer prophylaxis (SUC) with sucralfate (n = 48) with that of acid neutralizing prophylaxis (AN) utilizing antacids and cimetidine (n = 48) in the prevention of stress ulcer bleeding and nosocomial pneumonia (PN) in thermally injured patients. In the subset of intubated patients, the incidence of PN was 17.8% and 42.8% in the AN and SUC groups, respectively ($p < 0.05$) despite a similar postburn time of onset of pneumonia. Ten patients in each group died. Three patients in the SUC group developed upper GI bleeding with one requiring gastrectomy. Bacterial colonization of the upper airway occurred in virtually all patients, whereas 83% (SUC) and 96% (AN) had colonization of gastric contents. Gram-negative colonization rates for the upper airway were not different (70%) whereas 48% of SUC patients compared with 60% of AN patients had gram-negative gastric colonization. In conclusion, SUC therapy was efficacious in the prevention of stress ulcer bleeding but did not alter the rate of bacterial colonization of the airway or gastric contents, and was associated with a higher incidence of nosocomial pneumonia in intubated patients.

BEFORE THE ADOPTION of measures to neutralize gastric acid, gastrointestinal bleeding was a common and lethal complication in thermally injured patients. Endoscopically documented mucosal ulcerations could be identified in up to 90% of patients with burns of 35% or more of the body surface, and in up to one quarter of these patients clinically important bleeding occurred that was associated with mortality rates of 50% to 70%.[1-3] Therapy aimed at maintaining gastric pH above 4.5 virtually eliminated this complication.[4,5]

Neutralization of gastric acid allows the stomach contents to become rapidly colonized with bacteria, principally gram-negative organisms. In 1978, Atherton and White proposed that the stomach might serve as a reservoir for bacteria that subsequently colonized and infected the respiratory tracts of mechanically ventilated patients.[6,7] Recent reports have suggested that stress ulcer prophylaxis that does not result in gastric alkalinization may decrease the risk of nosocomial pneumonia, principally by decreasing gastric bacterial colonization.[8-11]

Nosocomial pneumonia is the most frequent life-threatening infection that occurs in thermally injured patients. Pulmonary infection was responsible for 42% of deaths that occurred in our burn center between 1987 and 1991.[12] In the past we have identified that the major risk factors for the development of pulmonary infection are the presence of inhalation injury requiring mechanical ventilatory support, age, and extent of burn.[13] Some authors suggest that standard stress ulcer prophylaxis regimens that neutralize gastric acid should be added to this list.[14]

The current study was designed to compare the efficacy of non-acid neutralizing stress ulcer prophylaxis using sucralfate with that of conventional acid neutralizing therapy in the prevention of stress ulcer-induced GI bleeding and nosocomial pneumonia in critically ill, thermally injured patients.

PATIENTS AND METHODS

Study Design

All adult burn patients (18 year old)admitted to the United States Army Institute of Surgical Research within 48 hours of injury with greater than a 20% total body surface area burn were considered for entry into this study. Patients with a prior history of peptic ulcer disease, preinjury H_2 receptor antagonist therapy, or a diagnosis of pneumonia at the time of admission

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were excluded from enrollment. Consenting patients were randomized in a pairwise fashion to receive either acid neutralizing stress ulcer prophylaxis consisting of cimetidine and antacids (AN) or non-acid neutralizing therapy using sucralfate (SUC). Cimetidine was administered every 6 hours at a dose of 300 mg. The dose was subsequently adjusted depending upon patients' renal function and gastric pH. Antacids were administered as a 30-mL bolus orally or via nasogastric tube every 2 hours. Gastric pH was measured every hour using pH paper or an indwelling gastric pH probe (both were calibrated against reference standards) and if the pH was less than 4.5, the dose of antacids was doubled or administered on an hourly basis. If this failed to increase gastric pH above the threshold level, the cimetidine administration was changed to a continuous infusion. Sucralfate, 1 g suspended in 20 mL of water, was administered orally or via nasogastric tube every 6 hours. The tube was clamped for 1-hour following administration.

All patients were resuscitated using the modified Brooke formula. Inhalation injury was diagnosed by bronchosopy or xenon ventilation/perfusion scanning. Wound care consisted of alternating silver sulfadiazine and mafenide acetate with excision and grafting initiated within the first postburn week. Continuous enteral feedings were begun on postburn day 3 at a rate sufficient to meet peak metabolic demands if the patient was unable to meet requirements orally.

All patients with gross clinically evident upper GI bleeding underwent endoscopy to verify the source of bleeding. Evidence of clinically apparent stress ulceration was considered a treatment failure.

Infectious Complications

The diagnosis of pneumonia was based upon roentgenographic findings consistent with pneumonia, sputum leukocytosis greater than 25 white cells per high-power microscopic field, and growth of a predominant organism on sputum sample culture. Chest roentgenograms were reviewed by a staff surgeon and a radiologist who were unaware of the patient's treatment group. Gram's staining and cultures of sputum samples and gastric aspirate cultures were obtained every Monday, Wednesday, and Friday, and as clinically dictated. The isolates from each source were typed and compared. The timing of colonization for each source was recorded.

Data Analysis

The age, total body surface area burned, presence of inhalation injury, requirement for intubation and ventilatory support, length of intubation, presence of pneumonia, postburn day of diagnosis of pneumonia, and outcome were recorded for all patients. All data are presented as the mean ± standard error of the mean, and were analyzed by Chi-square or unpaired Student's t test when appropriate. Logistic regression analysis was performed to identify the factors associated with the development of pneumonia or mortality. All analyses were performed using the BMDP statistical package.

RESULTS

From March 1990 through December 1992, 100 patients were randomized into this study, with 50 receiving acid neutralizing therapy and 50 non-acid neutralizing prophylaxis. There were two protocol violations in each group, leaving a total of 96 patients for evaluation. Demographic data are displayed in Table 1. There were no significant differences in age, burn size, the presence of inhalation injury, requirements for intubation, or outcome between the two groups. The groups were compared using a severity index based upon age, burn size, and the presence of inhalation injury.[13] The severity findings were not different between groups, indicating the similarity of the patient cohorts.

Table 1
Patient cohorts

	Acid Neutralizing Treatment (n = 48)	Sucralfate Treatment (n = 48)
Age (years)	37.6 ± 2.5	36.7 ± 1.99
TBSA (%)	49.3 ± 2.9	46.5 ± 3.5
Inhalation injury	22 (45%)	27 (56%)
Intubation	29 (60%)	28 (58%)
Mortality (%)	20.8	20.8
Severity index	28.28	33.37

TBSA = Total body surface area burned.

Table 2
Inhalation injury patients

	Acid Neutralizing Treatment (n = 22)	Sucralfate Treatment (n = 27)
Age (years)	40.8 ± 4.1	36.3 ± 2.3
TBSA (%)	50.6 ± 4.4	60.3 ± 4.6
Intubation	20 (91%)	22 (81.4%)
Mortality (%)	27.2	29.6
Severity index	45.63	50.96

TBSA = Total body surface area burned.

Table 3
Intubated patients

	Acid Neutralizing Treatment (n = 29)	Sucralfate Treatment (n = 28)
Age (years)	40.1 ± 3.7	36.4 ± 2.5
TBSA (%)	54 ± 4.1	63 ± 4.2
Inhalation injury	21 (72%)	22 (78.5%)
Mortality (%)	27.6	32
Severity index	45.66	55.02

TBSA = Total body surface area burned.

Since both the presence of inhalation injury and the requirement for intubation are significant risk factors for the development of nosocomial pneumonia, patients were further segregated based upon these two factors. Tables 2 and 3 contain the demographic data for patients in each cohort segregated by their prophylaxis regimens. There were no discernible differences between groups in each cohort. In the intubated cohort, the severity indices of 0.4566 and 0.5502 for AN and SUC, respectively, were not significantly different since the 95% confidence limits overlapped.

Clinically apparent upper gastrointestinal tract bleeding developed in three patients receiving sucralfate and in no patients receiving AN. One patient in the sucralfate group required a gastrectomy for control of hemorrhage.

Pneumonia occurred at a greater frequency in the

sucralfate group compared with the acid neutralizing group, although the difference was not statistically significant (Table 4). This same trend persisted in the inhalation injury and intubation cohorts. Of particular note was the incidence of pneumonia that occurred while patients were intubated: 42.8% of the sucralfate group and 17.9% of the acid neutralizing group developed pneumonia while intubated, a difference that was statistically significant. The PBD of diagnosis of pneumonia was identical between the two groups: 23.3 ± 10 days in AN and 23.8 ± 6.8 days in the sucralfate group. Not surprisingly, the duration of intubation was longer in the sucralfate group, presumably related to the higher incidence of pneumonia (13.5 ± 2.5 days vs. 22.3 ± 5.2 days). The types of organisms causing pneumonia in each group are shown in Table 5. Although SUC treatment tended to have a higher proportion of gram-positive pneumonias compared with AN treatment, this difference was not statistically significant.

The percentages of patients in each group who developed positive sputum or gastric cultures for any bacteria, and gram-negative bacteria specifically, are shown in Table 6. The incidence of sputum colonization was identical between the two groups, whereas there was a small but not significant decrease in gastric colonization rates in the sucralfate group compared with the acid neutralizing group. The postburn day of colonization of the sputum samples for any bacteria and gram-negative bacteria specifically in AN and SUC were not statistically difference (1.7 ± 0.2 days vs. 1.89 ± 0.35 days, and 7.73 ± 2.5 days vs. 9.36 ± 3.7 days, respectively). The postburn day of intragastric colonization was nearly identical, although the postburn day of gram-negative colonization was nearly twice that in the sucralfate group compared with the acid-neutralizing group (2.02 ± 0.22 days vs. 2.89 ± 0.78 days and 4.1 ± 0.49 days vs. 7.26 ± 1.5 days, respectively).

The highest and lowest gastric pH values were recorded each day in all patients. The mean high gastric pH was 7.11 ± 0.3 and 5.77 ± 0.4 in the AN and SUC groups, respectively. The mean low gastric pH was 3.74 ± 0.6 and 3.03 ± 0.1 in the AN and SUC groups, respectively. Hourly gastric pH was recorded in 13 AN patients and six SUC patients. In the AN group, 18% of the readings were less than 4.0. Surprisingly, only 36% of the SUC readings were less than 4.0, despite the lack of acid neutralization therapy.

There were nine deaths before postburn day 5: five in the acid-neutralizing group and four in the sucralfate group. None of these patients developed pneumonia. In general, these were patients with large burns and severe inhalation injuries who did not live long enough to be at risk for the development of pneumonia. Exclusion of these patients from analysis did not alter the above findings.

Table 7 compares the patients with and without pneumonia irrespective of their prophylaxis regimen. Patients who died before postburn day 5 were excluded from this analysis, because none of these patients developed pneumonia, and the PBD of death was significantly earlier than the mean postburn day of diagnosis of pneumonia. As expected, the patients who developed pneumonia were older ($p = 0.07$), had larger burns ($p < 0.0001$), and had a higher incidence of inhalation injury ($p < 0.001$) and intubation ($p < 0.01$). Although mortality was greater in

Table 4
Incidence of pneumonia

	Acid Neutralizing Treatment	Sucralfate Treatment
All patients	18.7% (9)	35.4% (17)
Inhalation injury		
Yes	31.8% (7/22)	48% (13/27)
No	7.5% (2/26)	19% (4/21)
Intubated		
Yes	28% (8/29)	57% (16/28)
No	5.3% (1/19)	5% (1/20)
While intubated	17.9% (5/29)	42.8% (12/28)*

* $p < 0.05$.

Table 5
Type of pneumonia

	Acid Neutralizing Treatment	Sucralfate Treatment
Gram positive	11% (1)*	29% (5)
Gram negative	33% (3)	12% (2)
Mixed	56% (5)	59% (10)

* Number of patients in parentheses.

Table 6
Colonization rates (%)

	Acid Neutralizing Treatment	Sucralfate Treatment
Sputum		
Any	100	98
Gram-negative	70	70
Gastric		
Any	96	83
Gram negative	60	48

Table 7
Comparison of patients without and with pneumonia

	No (n = 61)	Yes (n = 26)
Age (years)	34.3 ± 1.8	40.2 ± 2.7
Total body surface area burned (%)	38.5 ± 2.3	59.7 ± 3.8*
Inhalation injury (%)	39.3	76.9*
Intubation (%)	39.3	92.3*
Length of intubation (days)†	12.1 ± 2.6	29.1 ± 5.5*
Length of intubation before pneumonia (days)	—	10.9 ± 1.9
Mortality (%)	9.8	19.2

* $p < 0.05$ compared with no pneumonia.
† Mean ± SEM only for intubated patients.

these patients the difference was not statistically significant, possibly secondary to a type II error.

A stepwise logistic regression analysis was performed to determine which factors were correlated with the development of pneumonia. That analysis revealed that increasing patient age and extent of burn as well as the requirement for intubation were independently associated with the development of pneumonia, whereas the presence of inhalation injury and the type of stress ulcer prophylaxis therapy were not. Logistic regression analysis was also performed to identify the factors associated with a fatal outcome. Not surprising, age, extent of burn, and the development of pneumonia were significant predictors of death, whereas intubation, inhalation injury, and type of stress ulcer prophylaxis were not.

DISCUSSION

Thermally injured patients represent a population at significant risk for the formation of gastric stress ulcers. In 1974 Czaja and colleagues reported that gastric mucosal lesions can form within minutes to hours following injury, and that the incidence approaches 100% in patients with serious burns.[1] Before the institution of prophylactic therapy, clinical complications occurred in 28% of patients, with 13% requiring surgical intervention. The recognition that acid was a prerequisite for the development of gastric mucosal injury led to the initiation of antacid therapy for prophylaxis.[4] The advent of histamine H_2 receptor antagonists added another option and these agents, either alone or in combination, have significantly reduced the incidence of stress ulcers to less than 2% of all burn patients.[15]

Those data led to the institution of our current regimen for prophylaxis consisting of both antacid and H_2 antagonist therapy. The success of this approach requires assiduous titration of gastric pH to greater than 4.5. Failure to achieve pH control when using acid neutralization prophylaxis leads to an unacceptable rate of upper GI bleeding, as documented by Laggner et al.[16] In their study, failure to increase gastric pH using bolus infusions of ranitidine resulted in a 43.7% incidence of bleeding in a group of patients requiring long-term ventilation. Such a treatment regimen is labor intensive, exposes caregivers to patient secretions, and results in an unacceptable level of side effects if either agent is employed alone. In our experience, the side effects associated with the use of these agents may be limited by the simultaneous use of both, thus decreasing the necessary dose of each.

Despite this success, such a regimen recently has been implicated as unnecessarily exposing patients to an increased risk of nosocomial pneumonia.[17,18] In light of that possibility and the diminishing incidence of stress ulcers some have suggested that prophylaxis is unnecessary.[19,20] Although not specifically addressed in our study, two meta-analyses have clearly demonstrated that acid neutralization prophylaxis significantly decreases the incidence of gastric bleeding in both surgical and medical ICU patients compared with placebo therapy.[21,22] Thus it is clear that some form of prophylaxis is appropriate. It is unquestioned that maintaining the intragastric pH greater than 4.5 results in bacterial colonization of stomach contents.[23,24] The hypothesis that such overgrowth leads to an increased incidence of nosocomial pneumonia prompted a search for an alternative method of stress ulcer prophylaxis that did not alter gastric pH. Sucralfate, a chemical complex of sucrose octosulfate and aluminum hydroxide, appears to protect against stress ulceration through pepsin absorption, mucosal protein binding, and cytoprotection, presumably via increased local prostaglandin production, without significantly altering gastric pH.[25,26] Hypothetically, such a compound should reduce the incidence of nosocomial pneumonia by decreasing colonization of gastric contents.

In 1987 Tryba compared sucralfate with antacid prophylaxis in a series of surgical ICU patients requiring mechanical ventilation and found a threefold greater incidence of pneumonia in the patients receiving antacids.[9] In that same year, Driks et al. reported that sucralfate-treated patients had a lower incidence of nosocomial pneumonia than patients treated with either antacids or H_2 antagonists alone or in combination.[8] However, when the latter study is carefully examined, only patients treated with antacids had a higher incidence of pneumonia. Since 1987 there have been multiple studies comparing various regimens of non-acid neutralizing prophylaxis with acid neutralizing regimens. Many of these studies have similar shortcomings in that heterogeneous patient populations with relatively small numbers of patients were studied.[11,27] Indeed, two recent meta-analyses have offered conflicting conclusions as to which type of regimen is superior.[28,29] It is probable that the conflict between the two meta-analyses can be explained by the combining of trials involving heterogeneous patient groups with poorly matched patient cohorts in which many different prophylaxic regimens were employed. In a recent well controlled, randomized prospective trial comparing sucralfate with either bolus or continuous cimetidine administration in nonburned trauma patients, Fabian et al. found no difference in the incidence of nosocomial pneumonia.[30]

Our study represents a relatively homogeneous patient population in which the severity of the precipitating insult can be easily indexed, i.e., extent of burn and the presence or absence of inhalation injury. In this patient population, sucralfate prophylaxis did not result in a lower incidence of nosocomial pneumonia but, in fact, in the patients requiring intubation, was associated with a higher incidence of pneumonia during the period of ventilatory support. Fabian and colleagues indicted antacid prophylaxis as the agent responsible for the increase in nosocomial pneumonia reported in some series and thus their trial of cimetidine versus sucralfate would not have been expected to show any difference.[30] In our trial, as

in that of Simms and colleagues,[31] this was not found to be true. In both studies, antacids were not associated with an increase in the frequency of pneumonia. Furthermore, although acid neutralization appears to hasten gastric colonization with gram-negative bacteria, no association with frequency of organism-specific pneumonia could be identified. The absence of a relationship between gastric colonization and subsequent tracheal colonization and nosocomial pneumonia has also been reported in postoperative neurosurgical patients receiving ranitidine and antacids as well as a group of ventilated general ICU patients receiving selective gut decontamination.[23,24]

In an attempt to reconcile the conflicting literature, Tryba and colleagues have reviewed many of the recently published studies.[14] They concluded that since only some populations are at risk for the development of nosocomial pneumonia via the gastropulmonary route only they would benefit from non-acid neutralizing prophylaxis regimens. Such groups consist of surgical and trauma patients, patients receiving anti-ulcer prophylaxis for more than 7 days, patients receiving high-dose antacid therapy with pH titration, patients receiving continuous enteral nutrition, and patients requiring mechanical ventilation for more than 4 days. Other high-risk groups consist of patients with a pneumonia rate that exceeds 20% and those with an increase in gastric colonization during acid neutralization therapy. Our patient population meets the majority of these criteria, and yet we found no benefit from the use of non-acid neutralizing therapy. Moreover, recent reports impugn several of the proposed criteria. First, two recent studies in trauma patients have shown early continuous enteral nutrition to result in a lower, not higher, incidence of both pulmonary and total infectious complications.[32,33] Second, Simms' study clearly showed a higher incidence of gastric colonization but no resultant increase in pneumonia rates when acid neutralizing prophylaxis was employed.[31]

In a recent communication, Tryba redefined the "high-risk" factors, to include "surgical patients receiving long-term mechanical ventilation and those with low basic pH and no continuous enteral feedings."[34] Our limited pH data suggest that critically ill burn patients have gastric pH in excess of 4 a significant portion of the day. Thus, according to Tryba, the result of our study was "predictable." Since many similar studies, including ours and that of Fabian, report gastric pH to be elevated for a significant portion of the day in critically ill surgical patients not receiving AN, it would appear that the population at risk as defined by Tryba would be quite small. Nonetheless, these same patients have occasional measured gastric pH levels that are also quite low, indicating the requirement for some form of prophylaxis.

Our multivariant analysis indicated that injury severity and requirements for intubation but not stress ulcer prophylaxis regimens were related to the development of nosocomial pneumonia. Inhalation injury was not specifically related to the development of pneumonia, presumably because intubation, an event that is required in approximately 90% of inhalation injury patients, is more strongly associated with the development of pneumonia. This refines the predictive value of inhalation injury alone since only the most severly injured patients require intubation. Fabian et al. reported similar findings, indicating that in trauma patients injury severity, including measures of CNS injury but not stress ulcer prophylaxis regimens, were directly related to nosocomial pneumonia rates.[30] Our finding of a significant increase in the incidence of pneumonia in patients while intubated in the sucralfate group reflects a limitation of univariate analysis in assessing the importance of risk factors associated with the development of pneumonia. When we utilized multivariate analysis, sucralfate therapy was not associated with an increased risk of pneumonia, possibly indicating that the intubation cohorts were not as evenly matched as univariate analysis indicated. This is further supported by comparison of the severity indices, which indicated that the sucralfate group tended to be somewhat more severely injured than the acid neutralizing group. The frequency of pneumonia as a serious comorbid factor in patients with burns and those with other injuries justifies careful study of therapies that may decrease the incidence of this life-threatening complication. Our data and a review of other well designed trials involving trauma patients indicate that there is no benefit from the use of non-acid neutralizing prophylaxis in the prevention of gastric stress ulcerations and subsequent nosocomial pneumonia.[30,31] The occurrence of clinically significant upper gastrointestinal bleeding in three patients in the sucralfate group, in one of whom surgical control was required, is alarming even though the small number of study patients prevented such from attaining statistical significance. That failure rate in combination with lack of prophylactic regimen effect on the incidence of pneumonia speaks for our continued preference for acid neutralizing regimens of upper gastrointestinal stress ulcer prophylaxis.

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DISCUSSION

Dr. Philip S. Barie (New York, New York): This study was generally well designed, well performed, and very well presented. The authors are to be commended.

The authors have shown no difference between aluminum sucrose octosulfate (sucralfate) and pH control with combined antacid and H_2-antagonist receptor therapy on the incidence of pneumonia. Notably, they have done so in a relatively homogeneous patient population and in a group of patients at theoretically very high risk of pneumonia in that more than one half of their evaluable patients had inhalation injury. This paper presents, in my view, the highest risk group of patients in which such a study has been done.

Although post-hoc subgroup analysis revealed some differences, most notably a significantly higher rate of pneumonia in intubated patients who received sucralfate, I believe the take-home message is that prophylaxis for stress gastritis does not impact the pneumonia rate. As Doctor Cioffi has pointed out, his sucralfate patients were probably a bit sicker. Most studies of this type do not show a trend toward higher pneumonia rates with sucralfate therapy. Alarmingly, the authors noted three patients with serious bleeds in the sucralfate group, one of whom required gastrectomy. This conforms to our own casual observations.

I would like to place the paper in perspective with respect to its two primary design limitations: number one, that antacids and H_2 blockers were given together rather than separately, and number two, that the diagnosis of pneumonia on standard clinical grounds leaves much to be desired. [Slide] This is a summary of the two meta-analyses, both published within months of each other in 1989, which led to this whole debate.

The first was in *Critical Care Medicine*, in aggregate looking at about 12 studies. This paper had a major methodologic flaw in that data from three abstracts without peer review of any type were included in the meta-analysis.

The second paper, published in *Chest*, was more forthright in its analysis of the data that were included. Without going into the methodologic limitations of meta-analysis, some of which are quite exciting, only eight of 48 of these stress ulcer prophylaxis papers talked about pneumonia. The papers included were of widely disparate qualities, studied selected rather than randomized patients in three of the eight reports with randomized studies, and in none was there blinding of either the radiologist or the treating clinician as to the status of pneumonia. Interestingly, they found that antacid prophylaxis, contrary to belief at the time, did not increase the incidence of pneumonia.

This study has been done in a homogeneous patient population, which I think is one of the major strengths of the study. This literature in general has suffered from the fact that these studies have been done in a widely disparate patient populations. The diagnostic criteria for pneumonia have been a major problem. And, of course, the presence of not only an endotracheal tube but a nasogastric tube may confound the results.

One potentially important aspect that has not really been discussed is what happens when sucralfate itself is aspirated. [Slide] This is a study from the anesthesia group at Harvard in which they used three groups of rats, and put sucralfate or saline into a fresh tracheostomy. The sucralfate was buffered to two different pH levels. They found evidence of a fairly severe pulmonary parenchymal injury, so sucralfate into the lungs appears not to be benign, either.

[Slide] Nosocomial pneumonia is a difficult diagnosis to

make. This is one of the limitations of virtually all of these studies, in that clinical criteria are used while the state of the art, at least for pneumonia research, has progressed.

This paper appeared in *Chest* in 1993. It is from a Belgian group that is one of the leaders in clinical research in nosocomial pneumonia, particularly using the protected specimen brush catheter. They did a prospective study of 84 patients and asked themselves how good they were at determining whether patients had pneumonia. In fact, they were accurate only 62% of the time when compared with predefined rigid criteria. The residents were as accurate as the staff physicians, and unanimous assessments were incorrect 10% of the time. Thus, even for experienced physicians, nosocomial pneumonia is a difficult diagnosis to make.

[Slide] Putting Doctor Cioffi's data, as well as the results of two other recent surgical studies performed by our colleagues Doctor Simms and Doctor Fabian, in perspective, you can see that the incidence of pneumonia is the same for sucralfate versus pH control (30% vs. 27%). If these studies are added to the previous meta-analyses the argument that sucralfate lowers the nosocomial pneumonia rate essentially evaporates.

I would like to ask Doctor Cioffi three questions. Number one, did you control or look at pH in your sucralfate group? Sucralfate has been reported to be a weak agonist of duodenal bicarbonate secretion. Number two, do you believe the lingering perception in the literature that antacids and H_2 blockers may pose different risks? Also, in the future would you consider making some attempt to quantitate nosocomial pneumonia using such techniques as the protected specimen brush or bronchoalveolar lavage? Thank you.

Dr. William G. Cioffi (Closing): Thanks, Doctor Barie, for your discussion. We did measure gastric pH in both of our groups. We recorded for all 96 evaluable patients the highest and lowest pHs of the day and we also recorded hourly pH data on a smaller subgroup of the patients.

In terms of the smaller subgroup, we found that in the sucralfate group only 38% of the time was the pH less than 4 despite the lack of acid neutralization, whereas that was true 18% or 19% of the time in the acid neutralization group. In terms of the patients as an aggregate, the low pH in the sucralfate group averaged approximately 3.3 and the high just over 5. In the acid neutralization group the lowest pH averaged just under 4 and the high near 6.

So it was apparent to us that despite the lack of acid neutralization therapy administered by us that critically ill burn patients spent a considerable portion of their day with their gastric pH above 4. That is potentially the explanation for why our colonization rates were similar.

Why did we use antacids and H_2 blockers together? That has been our standard therapy for more than a decade and has led to our clinical success in eradicating stress ulcers as a complication in burn patients. Thus we wanted to study what we do clinically in our patients with what was in the literature.

In terms of antacids having been implicated both in Doctor Fabian's and in Doctor Tryba's papers as being responsible for the increased incidence of pneumonia because of the volume of antacids required to increase gastric pH, I think our data put that issue to rest.

And finally, pertaining to the diagnosis of pneumonia, we struggle, like all ICUs, in finding the right way to make the diagnosis. We have tried various other methods, but unlike our European colleagues we have not found any benefit of protected brush specimens or BAL or anything else, in terms of being that much better.